

### AMENDMENTS TO THE CLAIMS

1. (Currently amended) A nucleic acid probe ~~comprising an end which is labeled with a fluorescent dye, and in which fluorescence of the fluorescent dye decreases upon hybridization, wherein the nucleic acid probe has~~consisting of a nucleotide sequence ending at the nucleotide number 196 in the nucleotide sequence of SEQ ID NO: 2 and having a length of 7 to 30 nucleotides, ~~and the 3' end of~~wherein position 196 of the probe is cytosine labeled with the a fluorescent dye.

2. (Previously presented) The nucleic acid probe according to claim 1, wherein the nucleic acid probe has the nucleotide sequence of SEQ ID NO: 8.

3. (Currently amended) A method for detecting a mutation comprising  
hybridizing a probe consisting of a nucleotide sequence ending at the nucleotide number 196 in the nucleotide sequence of SEQ ID NO: 2 and having a length of 7 to 30 nucleotides with a nucleic acid having a single nucleotide polymorphism site at position 64 in the amino acid sequence of the  $\beta$ 3-adrenergic receptor, wherein position 196 of the probe is cytosine labeled with a fluorescent dye,

performing a melting curve analysis for a nucleic acid having a single nucleotide polymorphism site by using a nucleic acid probe labeled with a fluorescent dye, and

measuring fluorescence of the fluorescent dye, and

detecting the mutation on the basis of the result of the melting curve analysis, wherein the single nucleotide polymorphism is a mutation in a polynucleotide encoding a the  $\beta$ 3-adrenergic receptor, resulting in a mutation replacing tryptophan at position 64 in an the amino acid sequence of the  $\beta$ 3-adrenergic receptor with arginine, and the nucleic acid probe is defined in claim 1 and wherein the method is capable of detecting copy number as low as 20 genomic copies.

4. (Previously presented) The method according to claim 3, wherein a region containing the single nucleotide polymorphism site in a polynucleotide contained in a sample is amplified to obtain the nucleic acid showing the single nucleotide polymorphism.

5. (Previously presented) The method according to claim 4, wherein the amplification is performed using a DNA polymerase.

6. (Original) The method according to claim 5, wherein the amplification is performed in the presence of a nucleic acid probe.

7. (Currently amended) A kit ~~for the method as defined in claim 3, comprising a nucleic acid probe comprising an end which is labeled with a fluorescent dye, and in which fluorescence of the fluorescent dye decreases upon hybridization, wherein the nucleic acid probe has a nucleotide sequence ending at the nucleotide number 196 in the nucleotide sequence of SEQ ID NO: 2 and having a length of 7 to 30 nucleotides, and the 3' end of the probe is labeled with the fluorescent dye according to claim 1.~~

8. (Previously presented) The kit according to claim 7, wherein the nucleic acid probe has the nucleotide sequence of SEQ ID NO: 8.

9. (Previously presented) The kit according to claim 7, which further comprises a primer for amplifying a region containing a mutation in a polynucleotide encoding a  $\beta$ 3-adrenergic receptor, resulting in a mutation replacing tryptophan at position 64 in an amino acid sequence of the  $\beta$ 3-adrenergic receptor with arginine, by using a DNA polymerase.

## SUMMARY OF INTERVIEW

### Attendees, Date and Type of Interview

The interview was conducted on June 9, 2008 and attended by Cynthia Wilder and Chereskin.

### Exhibits and/or Demonstrations

none

### Identification of Claims Discussed

Claims 1, 3, and 7

### Identification of Prior Art Discussed

Lander, et al.

Buck, et al

Hiratsuka

### Proposed Amendments

Proposed amendments to claims 1 and 7 were faxed to the Examiner prior to the interview for discussion.

### Principal Arguments and Other Matters

Applicant's representative argued that Lander et al. do not teach Applicant's sequences and proposed to amend to "consisting of" language.

While Buck, et al. is cited for teaching equivalence of primers, Applicant's claimed invention is directed to probes, not primers. Any extrapolation of the teaching of Buck, et al. on primers to probes is rebutted by the teaching of the specification that shows that not all probes work equally well. Buck, et al also is directed to sequencing, not Tm analysis.

Hiratsuka teaches melting point analysis, but does not teach the importance of the label at the terminal cytosine at the 3' end (position 196) and does not teach the specific mutation. Additionally, the claimed invention is nonobvious in view of the cited references because the

**Application No.:** 10/553,509  
**Filing Date:** October 18, 2005

method is sensitive (Figure 5) and reproducible (Figure 6) down to low copy number (20 genomic copies).

None of the references teach the polymorphism at position 64.

The Examiner suggested introduction of active steps into the method claims (claim 3) and that the low copy number detectable by the method as disclosed in the specification may be a patentable feature.

#### Results of Interview

Applicants will consider submission of amendments as discussed during the interview.